Remarks

The Office Action mailed 28 July 2005 has been received and reviewed. Claims 34 and 71-82 having been amended, and new claims 83 and 84 having been added, the pending claims are claims 34-84. Claims 45-66 and 70 having been withdrawn, the claims currently under examination are claims 34-44, 67-69, and 71-84. Support for amended claim 34 and new claim 84 is found, for example, on p. 6, lines 12-14, of the specification. Support for new claim 83 is found, for example, on p. 8, lines 4-11, of the specification. Reconsideration and withdrawal of the rejections is respectfully requested.

The Examiner requested that claims 70-82 be withdrawn, as the claims are directed to a non-elected species; namely, siderophore receptor protein from a gram-positive species. Applicants have withdrawn claim 70, and amended claims 71-82 to be dependent on generic claim 69. Applicant submits that if a determination of an allowable generic claim issues, the Examiner should advise Applicants that claims drawn to the non-elected species are no longer withdrawn since they are fully embraced by the allowed generic claim. M.P.E.P. § 809.02(c). Therefore, the Applicant respectfully requests that the Examiner consider rejoining the non-selected species upon a finding of allowability of generic claim 69.

Obviousness-Type Double Patenting Rejection

Claims 34-44 and 67-69 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,682,754. Applicants appreciatively note that claims 67-69 have not been rejected outside of the double patenting rejection. Upon an indication of otherwise allowable subject matter, and in the event this rejection is maintained, Applicants will provide an appropriate response.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 34, 37, and 39-43 under 35 U.S.C. §103(a) as being unpatentable over Emery et al. (U.S. Patent No. 5,830,479) in view of Phelps et al. (U.S. Patent No. 5,339,766). This rejection is respectfully traversed.

Applicants appreciate the Examiner noting that Emery et al. does not specifically teach administration of a siderophore receptor *in ovo* "at a time when maternal antibodies of the bird to the immunogen are sufficiently reduced." (Office Action mailed July 28, 2005), though Applicants note that *injection* of the immunogen, as recited by the claims, may occur well before a time when maternal antibodies to the immunogen are sufficiently reduced. The Examiner then asserts that Phelps et al. discloses a method for introducing material into poultry eggs *in ovo*, and that materials intended for delivery includes "vaccines, vitamins, antibiotics, hormone, enzyme inhibitors, peptides, cells, DNA and other therapeutic molecules."

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. *See* M.P.E.P. § 2143.

Applicants respectfully disagree that the Examiner has provided a *prima facie* case of obviousness, as the combination of Emery et al. with Phelps et al. does not teach or suggest all the claim limitations of claims 34, 37, and 39-43 . More specifically, the combination of Emery et al. with Phelps et al. does not provide "for sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen" (claim 34).

Emery et al. provides a vaccine composed of a substantially pure siderophore receptor protein that is useful for immunizing an avian or another animal against infection by gram-negative bacteria (see column 2, lines 13-27). Emery et al. further provides fourteen examples that describe the production and purification of siderophore receptor proteins, vaccination of turkey poults, and the ability of the siderophore receptor protein to provide cross-reactivity to

varying immunogens. As noted in the background, siderophores had previously not been utilized as immunogens due to an inability to extract these proteins.

Phelps et al., on the other hand, is not directed to the use of a novel immunogen, but rather provides "a method for injecting eggs to minimize the ingress of air and contaminants, and minimize the leakage of albumin from the egg." (column 3, lines 59-61). The method includes use of a sealant at the point of injection to prevent contamination and minimize leakage. While this is a useful method of administering a variety of materials to an egg, and is in fact incorporated by reference in Applicants' specification, this reference does not teach or suggest providing sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen.

The Examiner notes that "[i]t is well known in the art that newborn mammals such as poultry have weakened immune systems" (p. 7, lines 13-14) and later also states (on p. 8, lines 7-8) that "the ordinary artisan would have recognized that the most crucial time of vaccination delivery to a young bird is within the first few days of life." Applicants note that the Examiner is thus providing this information for use in the §103 rejection on the basis of being common knowledge in the art, in accordance with M.P.E.P. § 2144.03. Applicants further note that the M.P.E.P. further states, in § 2144.03, that "[i]t would not be appropriate for the examiner to take official notice of facts without citing a prior art reference where the facts asserted to be well known are not capable of instant and unquestionable demonstration as being well-known" and that "[i]t is never appropriate to rely solely on "common knowledge" in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based."

Applicants respectfully disagree with the statements that "[i]t is well known in the art that newborn mammals such as poultry have weakened immune systems" and that "the ordinary artisan would have recognized that the most crucial time of vaccination delivery to a young bird is within the first few days of life." First of all, while Applicant's assume this represents an oversight on the Examiner's part, it is noted that poultry are not mammals, and as such it is not possible for newborn *mammals such as poultry* to have weakened immune systems. More significantly, Applicants note that newborn avian hatchlings do not have a weakened immune

system *per se*, as maternally-derived antibodies provide immunological protection of the developing chick, but more precisely, as stated in Applicant's background, "[i]n the first few weeks of life a newborn chick, poult, duckling or other avian hatchling ("chick") is relatively incompetent at producing antibodies in response to antigenic stimuli" and that "[d]uring this period, a significant amount of resistance to infectious diseases is provided by passive immunity derived from maternal antibodies" (p. 1, lines 4-7 of the specification).

Applicants have described the complications in vaccination that result from the presence of maternal antibodies, noting that "the presence of maternal antibodies can interfere with the ability of young birds to actively respond to an immunogen" (p. 1, lines 16-18 of the specification). This bears directly on the Examiner's second contention; namely, that "the ordinary artisan would have recognized that the most crucial time of vaccination delivery to a young bird is within the first few days of life." Delivery of vaccine to a young bird within the first few days of life is *not* recognized to be a crucial time for vaccination, as the effect of vaccination at this time is suppressed by the presence of the maternal antibodies. Instead, "[i]n the poultry industry, conventional vaccination programs are designed to be administered after the decline of maternal antibody, typically starting at about 3-4 weeks of age" (p. 2, lines 7-9 of the specification). Thus, conventional wisdom is to deliver vaccine at 3-4 weeks of age, *not* during the first few days of life, as stated by the Examiner. However, as further noted by Applicants, vaccination is burdened by a number of problems, such as the difficulty of predicting exactly when the maternal antibodies have waned, requiring multiple administrations of the vaccine, which leads to further problems such as expense and stress on the birds. Applicants solution to this problem is injection of the vaccine *in ovo*, followed by sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen. Applicants respectfully assert that these elements of Applicants' claims are not provided by the combination of Emery et al. and Phelps et al., and further is not available as common knowledge.

Applicants further respectfully disagree that the Examiner has provided a *prima facie* case of obviousness, as the Examiner has not provided a suggestion or motivation to modify the

references or to combine the teachings of Emery et al. with Phelps et al. to provide a *prima facie* case of obviousness.

The Examiner has asserted that "one of ordinary skill in the art would have been motivated to administer a sustained-release formulation in ovo, to a bird (i.e., poultry such as chicken) wherein the formulation comprised a siderophore receptor such as enterochelin, and wherein the sustained-release formulation was sustained until the hatching of the bird (i.e., 1-60 or 1-90 days post hatching) in order to increase the bird's immune system to foreign disease causing bacteria" (p. 7, line 19 to page 8, line 3, Office Action mailed July 28, 2005). The basis of the motivation, as stated by the Examiner, appears to the found in the statement that "[i]t was clear from the prior art that siderophore receptors from gram-negative bacterial were known to vaccinate birds, and suggested for use in ovo by Emery et al." (p. 8, lines 3-4, Office Action mailed July 28, 2005). Emery et al. states that "[t]he vaccine may be delivered to the animal, for example, by parenteral delivery, injection (subcutaneous or intramuscular), sustained-released repository, aerosolization, egg inoculation (i.e., poultry), and the like" (column 11, lines 12-16). While Emery et al. briefly suggests egg inoculation, it does not suggest, or provide a motivation, to provide sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen, but rather merely suggests that the vaccine may be administered to eggs. Emery et al. is also silent with regard to the role of maternal antibodies and the development of the chick's immune system, and how this might influence the timing of vaccination.

There is further no motivation in Phelps et al. to provide sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen. As noted above, Phelps et al. discloses a method of introducing a substance into a bird egg utilizing a seal to minimize ingress of air and contaminants, and minimize the leakage of albumin from the egg. While Phelps et al. does make passing reference to the delivery of vaccines as one of the many substances that may be injected by this method, Phelps contains no suggestion or motivation to provide sustained release of the immunogen at least until the bird is

capable of mounting an immune response to the immunogen, and further contains no discussion of the role of maternal antibodies or the development of the chick's immune system.

To establish a *prima facie* case of obviousness, there must also be a reasonable expectation of success. A reasonable expectation of success is highly correlated to the predictability of the field of endeavor. Applicants respectfully suggest that immunization can be a highly unpredictable art, and that this unpredictability is further increased by the complex interaction between maternal antibodies and the newborn birds immune systems. Applicants, in the Examples (p. 27 to 35 of the specification) have demonstrated that in ovo immunization can be successfully carried out and that immunization in newborns can successfully occur due to sustained release of immunogen. Applicants respectfully suggest that a reasonable expectation of success did not exist prior to Applicant's disclosure, and is not provided by the combination of Emery et. al with Phelps et al.

Applicants respectfully disagree that the Examiner has provided a *prima facie* case of obviousness, for the reasons set forth above. Accordingly, Applicants request that the rejection of claims 34, 37, and 39-43 under 35 U.S.C. §103(a) be withdrawn.

The Examiner rejected claims 34-44 under 35 U.S.C. §103(a) as being unpatentable over Emery et al. (U.S. Patent No. 5,830,479) in view of Phelps et al. (U.S. Patent No. 5,339,766) and further in view of Evans et al. (U.S. Patent No. 6,500,438 B2). More specifically, the Examiner asserts that specific injection protocols, as recited by claims 35, 36, 38, and 44, are absent from the teachings of Emery et al. and Phelps et al., but are provided by Evans et al., citing column 2, lines 1-6, column 3, lines 25-27, and Example 1. To summarize the protocols provided by these claims; claim 35 recites injecting the implant during the fourth quarter of incubation of an egg; claim 36 recites injecting the implant at about 15-28 days of incubation of an egg; claim 38 recites injecting the implant at about 25-27 days of incubation of an egg wherein the bird is a turkey; and claim 44 further injecting the implant at about day 17 to 19 of incubation of an egg wherein the bird is a chicken. The rejection of claims 34-44 under 35 U.S.C. §103(a) is respectfully traversed.

Claims 34-44 are patentable over Emery et al. in vew of Phelps et al. for the reasons provided above. The disclosure of Evans et al. does not remedy the defects of Emery et al. or Phelps et al. Claims 35, 36, 38, and 44 are further patentable over Emery et al. and Phelps et al. in view of Evans et al. as the Examiner has failed to demonstrate that these claims are *prima facie* obvious.

The vaccination methods of Evans et al. are directed to the administration of *live* Eimeria spp sporozoites or merozoites, which are protozoal parasites that cause coccidosis. Live organisms provide a very different immune challenge compared with that provided by delayed and/or sustained release of siderophore receptor protein from an implant, and are of little value in predicting protocols that will be suitable for the siderophore receptor protein immunogens of the present invention. Accordingly, there is no reasonable expectation of success that administration of live protozoan parasites for vaccination against coccidiosis would make obvious Applicants' claims 34-44.

The Examiner asserts that "it would have been obvious to one of ordinary skill in the art ...to determine all operable and optimal concentration of components because concentration is an art-recognized result-effective variable which would have been routinely determined and optimized in the pharmaceutical art" (page 9, lines 13-17, Office Action mailed July 28, 2005). However, the additional limitations provided by claims 35, 36, 38, and 44 do not relate to concentration, and immunization is a medical art, but not a pharmaceutical art, as vaccines are not drugs. This assertion is thus not pertinent to the asserted obviousness of claims 34-44.

The Examiner further states that "although the prior art do not teach all the various permutation of injection times/release times, it would be conventional and within the skill of the art to identify the optional administration times as well as release times because (1) it is well known in the art that newborn mammals have weakened immune systems, (2) in-ovo administration of enterochelin to challenge the immune systems of incubating poultry embryos was clearly suggested by Emery et al and arginine and (3) sustained delivery systems for vaccines; i.e., biocompatible polymer coatings/matrices were well known and suggested for in-ovo delivery of vaccines" (p. 9, line 17, to page 10, line 2, Office Action mailed July 28, 2005).

Applicants respectfully disagree that the various permutations of injection times/release times are conventional and within the skill of the art to identify. The prior art contains examples of administration at various times, but the prior art does not describe providing sustained release of the immunogen at least until the bird is capable of mounting an immune response to the immunogen, and further contains no discussion of the role of maternal antibodies or the development of the chick's immune system. As the timing of administration and release plays an important role in providing immunogen "at least until the bird is capable of mounting an immune response to the immunogen," Applicants respectfully disagree that the injection times/release times are conventional and that Evans et al. supplants Emery et al. and Phelps et al. to provide a reasonable expectation of success regarding administration protocols.

Furthermore, the Examiner's assertion that Evans et al. "would have been effective during any time of incubation" is not supported. Column 2, lines 1-6 describes in ovo administration only during the final quarter of incubation. Example 1 describes injection only on day 18 of the incubation of chicken eggs. Column 3, lines 25-27 which refers to any time during incubation, refers to administration of *an immune stimulant* at any time, not administration of the vaccinating sporozoites or merozoites. Immune stimulants are described in column 6, lines 26-38, and include compounds such as cytokines and growth factors. Accordingly, Evans et al. does not teach or suggest all of the claim limitations provided by dependent claims 35, 36, 38, and 44, which the Examiner has stated are absent from Emery et al. and Phelps et al.

Furthermore, there is no motivation to combine the administration times of Evans et al. for use with Eimeria spp. sporozoites or merozoites with the siderophore vaccines of Emery et al. or the method of sealed injection provided by Phelps et al.

Applicant thus respectfully asserts that the Examiner has not made a *prima facie* case of obviousness for claims 34-44 under 35 U.S.C. §103(a) in view of Emery et al., Phelps et al, and Evans et al., and thus respectfully requests that the rejection of claims 34-44 over these references be withdrawn.

Summary

It is respectfully submitted that claims 34-44, 67-69, and 71-84 currently under examination are in condition for allowance, outside of the double patenting rejection Applicants have requested be temporarily held in abeyance, and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Daryll A. EMERY et al.

By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612) 305-1220
Facsimile: (612) 305-1228
Customer Number 26813

December 28, 2005
Date

By: David L Provence
David L. Provence
Reg. No. 43,022
Direct Dial (612) 305-1005

CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to **Mail Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 28th day of December ~~October~~, 2005, at 3:05 pm (Central Time).

By: Sue Dombroske
Name: Sue Dombroske